EXHIBIT 1

Evaluation of Bowel Distention and Bowel Wall Appearance by Using Neutral Oral Contrast Agent for Multi–Detector Row CT[1]

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Purpose: To prospectively evaluate the performance of an orally administered 0.1% barium suspension, Volumen, as a bowel-marking agent for multi–detector row computed tomography (CT).

Materials and Methods: This HIPAA compliant study was approved by the Institutional Review Board and conformed to the institutional standards for research funded by a commercial sponsor. A total of 60 patients (33 women, 27 men, average age, 58.2 years) who were referred for multi–detector row CT of the pancreas were randomized into two groups. Prior to examination, group 1 consumed 1200 mL of Volumen over a 30 minute period and group 2 consumed 1200 mL of a solution containing three parts water and one part methylcellulose over a 30-minute period. Results were independently reviewed by two radiologists who were unaware of the contrast agent used. The degree of distention and the visualization of mural detail were qualitatively scored on a five-point scale. Differences were evaluated by using the Mann-Whitney test at a confidence level of 95%.

Results: There was significantly better distention in the stomach ($P = .013$), duodenum ($P = .006$), jejunum ($P = .029$) and ileum ($P = .140$) in group 1 compared with group 2. Significant distention was also evident by comparing the products of the widest cross-sectional diameters in duodenum ($P = .143$), jejunum ($P < .001$), and ileum ($P < .001$). Group 1 also demonstrated significantly better visualization of mural features in the duodenum ($P = .003$), jejunum ($P = .024$), and ileum ($P = .01$) and a trend toward better visualization of mural features in the stomach ($P = .092$).

Conclusion: Oral administration of Volumen provided excellent distention and excellent visualization of mural features in the gastrointestinal tract.

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Multi-detector row computed tomographic (CT) scanners offer the ability to acquire image data composed of near-isotropic voxels that allow for high-quality and clinically useful volume imaging, thereby specifically enabling CT data (collected as a volume) to be viewed in any conceivable viewing plane (1). Volume imaging has several appeals. First, volume displays allow for the efficient communication of diagnostic information in displays that are more understandable to referring clinicians. Second, volume imaging allows for economic use of the larger data sets that result from scanners with more detector rows.

As volume imaging becomes increasingly used for primary diagnosis at CT, it is an opportune time to reevaluate the adjuncts that facilitate this imaging paradigm. Neutral endoluminal contrast agents (ie, contrast agents that afford the intestinal lumen an attenuation that is near that of water) could potentially improve diagnoses of abdominal and pelvic abnormalities at multi-detector row CT. Neutral contrast agents have been shown to be valuable in the diagnosis of small-bowel disorders, including ischemia (2), neoplasms (3), and Crohn disease (4-6), and have been used to mark the stomach and duodenum during evaluation of the pancreas and biliary tree (7,8). Most clinical experience is with plain water as a contrast agent. Water is an excellent contrast agent when used during upper abdominal CT scanning, but because water is rapidly absorbed through the intestinal wall, the use of this contrast agent in the jejunum and ileum is limited (7,8). Nasoenteric tubes have been proposed as a method to deliver contrast agents in a rapid bolus that would allow scanning prior to substantial absorption at CT enteroclysis (9,10). Patient acceptance, however, is markedly reduced because of the need for intubation and because of the increased time and materials associated with the procedure (5). Some investigators have suggested that water with suspending agents could produce high-quality peroral CT enterographic images (6,11).

The purpose of our study was to prospectively evaluate the performance of an orally administered 0.1% barium suspension, Volumen (E-Z-Em; Lake Success, New York), as a bowel-marking agent for multi-detector row CT.

Materials and Methods

The trial was sponsored by E-Z-Em. The sponsor provided the Volumen, and we provided the methylcellulose (E-Z-Em), Readi-Cat 2% (E-Z-Em), and glucagon (Glucagen; Bedford Laboratories, Bedford, Ohio). The sponsor created all data forms and instructed the physician assistants on the randomization process; the Institutional Review Board–approved consent form was used. The sponsor also made random visits to the site to provide quality control monitoring and oversight. The sponsor assumed the costs of the CT scans at the institutional research rate. The authors from New York University (A.J.M., E.M.H., J.J.C., J.S.B.) had sole control of the data generated by this trial. The authors who were employees of E-Z-Em (C.H., M.M.B., A.B.W.) were blinded to all data generated during the trial.

This study was compliant with the Health Insurance Portability and Accountability Act, was approved by the Institutional Review Board, and conformed to the institutional standards for research funded by a commercial sponsor. All patients enrolled in the study gave informed consent. The sponsor provided the mechanism for reporting adverse effects that were related to the contrast agent.

A total of 60 consecutive outpatients (33 women, 27 men; average age, 58.2 years) who were known to have or were suspected of having pancreatic or biliary disease were referred between December 2003 and May 2004 for evaluation with CT. Patients were randomized into two groups on the basis of the type of neutral oral contrast agent administered. Group 1 received 1200 mL of Volumen, and group 2 received 1200 mL of a solution containing three parts water and one part methylcellulose. Volumen contained additives in similar proportions to those contained in Readi-Cat 2%.

Demographically, 45 (75%) of the 60 patents enrolled in the study were white, seven (12%) were black, four (7%) were Hispanic, three (5%) were Asian, and one (2%) was not documented. The average age of was 58.2 years, average weight was 167.5 lb (76.0 kg), and average height was 66.4 inches (168.6 cm). Specific indications included known pancreatic disease, suspected pancreatic disease (ie, severe epigastric pain with or without weight loss), and biliary disease. Of the 60 patients who were included in the study, 26 (43%) had undergone previous abdominal surgery, including appendectomy, cholecystectomy, cystectomy with ileal conduit, hernia repair, hysterectomy, and colon resection. Surgical history was not documented in six patients (10%), and the remaining 28 patients (47%) had no history of abdominal surgery. A total of 42 patients (70%) were taking multiple medications at the time of their diagnostic procedure compared with 17 patients (28%) who were not on any medications at the time of their diagnostic procedure. Medication history was not obtained in one patient. Patients were excluded if they were known to have undergone prior pancreatic surgery, could not receive intravenous contrast material, or were unwilling to sign the institutional consent form.

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See Materials and Methods for pertinent disclosures.

An additional 60 consecutive outpatients (34 women, 26 men; average age, 64.0 years) who received Readi-Cat 2% were also included in our study. This portion of our study was Health Insurance Portability and Accountability Act–compliant and was approved by the Institutional Review Board, which waived informed consent.

Protocols: Contrast Agent Administration and CT Scanning

For each group, 900 mL of contrast agent was administered steadily for 20 minutes. After administration was complete, patients were asked to change into the examination gown and position themselves on the CT table. This interval was usually between 7 and 12 minutes. Once patients were on the table, an additional 200–300 mL of oral contrast agent was given. The total time for oral contrast administration varied between 27 and 32 minutes. The oral contrast material protocol for the additional 60 outpatients comprised the administration of 900–1000 mL of oral contrast agent over a 45-minute period. Immediately prior to scanning (ie, while the patient was on the CT table), an additional 200 mL of water was administered to distend the stomach.

A total of 14 examinations were performed with a four–detector row CT scanner (Volume Zoom; Siemens Medical Systems, Forchheim, Germany), and 46 examinations were performed with a 16–detector row CT scanner (Sensation 16; Siemens Medical Systems). All examinations were performed by using intravenous contrast material (Ultravist 300; Berlex Laboratories, Montville, NJ) that was administered by means of a power injector (Em Power; E-Z-Em) at rates of between 2 and 4 mL/sec. After localizer images were obtained, a dual acquisition protocol was used. Phase 1 (pancreatic phase) images were obtained 40 seconds after the initiation of the bolus from the xiphoid to the top of the sacroiliac joints by using a 4 × 1-mm detector configuration, creating 3-mm sections. Phase 2 (portal phase) images were obtained beginning at 75 seconds after the initiation of the bolus from the xiphoid to the symphysis pubis by using a 4 × 2.5-mm detector configuration, creating 4-mm sections. With the 16–detector row scanner, phase 1 images were obtained at 50 seconds with a 16 × 0.75-mm detector configuration, creating 3-mm sections, and phase 2 images were obtained at 90 seconds by using 16 × 1.5-mm detector configuration, creating 4-mm sections. For each acquisition, the coverage obtained with the 16–detector row protocol was identical to that obtained with the four–detector row protocol. A total of 46 (77%) of 60 patients (ie, 21 patients from group 1 and 25 patients from group 2) received 0.1 mg of glucagon immediately prior to CT scanning. Six patients (10%) (ie, two patients from group 1 and four patients from group 2) did not receive glucagon. Because glucagon administration was not documented in eight patients (13%), it was assumed that glucagon was not given.

CT Interpretation

Two attending radiologists (A.J.M., E.M.H.), one with more than 25 years experience and one with 2 years experience in dedicated body imaging, independently reviewed images from each examination as transverse 3- or 4-mm sections on a picture archiving and communication system workstation. Both readers were blinded to the type of oral contrast agent used. Images from each examination were rated on a continuous five-point scale (0 = worst, 4 = best) for the ability of the readers to visualize selected segments of the gastrointestinal tract (ie, gastric fundus, gastric antrum, duodenal folds, jejunal folds, and ileal folds) and for the qualitative assessment of distention in each segment (ie, stomach, duodenum, jejunum, and ileum). A score of 4 meant that the segment was distended, the wall was uniformly visualized, and a fold pattern could be recognized. A score of 0 meant that the segment was collapsed, the walls could not be seen, and a fold pattern could not be recognized. Readers did not have the ability to determine if the given segment was normal or possibly thickened from a pathologic process. Because the analysis was purposely qualitative, gradations from "total collapse, no folds seen, and no wall discerned" (ie, a score of 0) to "maximal distention, wall uniformly evaluated, and folds recognized" (ie, a score of 4) were collected on a continuous scale. Additionally, the readers were asked if there were diagnostic findings for each case and if there were other clinically important abnormalities present elsewhere on the images. Readers did not tabulate findings such as hepatic cysts, renal cysts, renal calculi, or gallstones.

A quantitative analysis of the degree of distention was also performed. One of the researchers (J.J.C., a 4th-year medical student) who was blinded to the contrast agent used measured the largest cross-sectional diameter from outer wall to outer wall within the duodenum, jejunum, and ileum for each patient. The largest diameter measurement (in square centimeters) could be chosen from either the phase 1 or phase 2 images. The product of the bidimensional measurements was tabulated for each segment in each patient. We similarly measured the largest cross-sectional diameters in the additional 60 consecutive outpatients who received Readi-Cat 2%. Our protocol for these patients was not modified from our normal oral dosing regimen, which comprised administration of 900–1000 mL of the oral contrast agent over a 45-minute period. Immediately prior to scanning (ie, while the patient was on the CT table), an additional 7 oz (207 mL) of water was administered to distend the stomach.

Statistical Analysis

In order to determine the statistical significance for qualitative analysis, an arithmetic mean of the numeric scores that were recorded by each reader for luminal distention and visualization of the stomach, duodenum, jejunum, and ileum was calculated. The arithmetic mean value for each reader was determined by averaging the responses to a visual assessment of distention in the stomach, duodenum, jejunum, and ileum, as recorded on a continuous five-point linear scale. Visualization was judged by each reader's ability to see the mural anatomic features that were appropriate to each specific segment. Gastric visualization was based on a combination of scores for the visualization of uniform thickness in the walls of the gastric fundus and gastric antrum. Visualization in the duodenum and jejunum was based on the subjective ability of readers to detect folds within these segments. Visualization in the ileum was based on the ability to see the ileal wall. The qualitative data points for distention and visualization in each segment for each patient were averaged for each of the two readers. The two groups (ie, group 1 and group 2) were then compared with respect to the mean values for each segment by using the Mann-Whitney test. These combined mean scores were compared at a 95% confidence level by using the Wilcoxon signed rank test.

For the quantitative analysis, a mixed-model least-squares regression was used to examine the differences among the contrast agents with respect to the product of the bidimensional diameter assessments. The dependent variable consisted of the product of the bidimensional measurements observed for each patient in each of the three regions of the small intestine (ie, duodenum, jejunum, and ileum). The prediction model included the contrast agent received by each patient (ie, Readi-Cat 2%, Volumen, or water with methylcellulose) and the location of each bidimensional assessment (ie, duodenum, jejunum, or ileum) as fixed classification factors, patient age and sex as covariates, and terms representing the interaction of contrast agent with location, age, and sex. The covariance structure was modeled by assuming that observations are either correlated or independent when associated with the same or different patients and by allowing the error variance to differ for each contrast agent.

Examination of the residuals from the mixed models that fit with the bidimensional assessments on the original scale of measurement suggested that the underlying model assumptions were reasonably met. Therefore, no normalizing or variance-stabilizing transformations were applied to the data. The mixed-model analysis indicated that the relative effects of the contrast agents on the bidimensional diameters were not the same in the three regions of the small intestine (ie, there was a significant interaction between region and contrast agent). Consequently, the Tukey honestly significant difference procedure was used to make all pairwise comparisons among the contrast agents with respect to their effect on diameter in each of the three regions while adjusting for the effects of age and sex and maintaining the familywise type I error rate for the set of comparisons at or below the nominal 5% level.

Table 1

Abnormalities Demonstrated at CT in Groups 1 and 2

Abnormality	Group 1	Group 2	Total
Pancreas-related			
Adenocarcinoma	2	2	4
Pseudocyst	2	2	4
Cystic mass	3	1	4
Chronic pancreatitis	2	2	4
Acute pancreatitis	0	1	1
Nonpancreas-related			
Lymphadenopathy	1	2	3
Small-bowel anastomoses	2	1	3
Diverticulosis	1	1	2
Mesenteric vein thrombosis	2	0	2
Cholangiocarcinoma	0	1	1
Duodenal lipoma	1	0	1
Duodenal diverticulum	0	1	1
Renal cancer	1	0	1
Polycystic kidney disease	1	0	1
Noncystic liver mass	1	0	1
Normal findings	11	16	27
Total	30	30	60

Note.—Data are the number of patients.

Results

Abnormalities Detected at CT

CT demonstrated abnormalities in 33 (55%) of 60 patients (Table 1). There were 17 pancreas-related abnormalities, including four adenocarcinomas, four cystic masses (in patients with no history of pancreatitis), four pseudocysts, four cases of chronic pancreatitis, and one case of acute pancreatitis. There was concordance between the two readers in 15 patients. In one patient, reader 1 interpreted the findings as pancreatic cancer, whereas reader 2 interpreted the findings as chronic pancreatitis. In a second patient, reader 1 failed to diagnose a cystic mass that was detected by reader 2. Abonormalites that were not related to the pancreas were observed in 16 patients, including three with lymphadenopathy, three with small-bowel anastomoses, two with diverticulosis, two with mesenteric vein thromboses, and one each with cholangiocarcinoma, duodenal lipoma, duodenal diverticulum, renal cancer, polycystic kidney disease, and noncystic liver mass.

Age and Sex

A total of 15 women and 15 men (mean age, 58.1 years) received Volumen; 18 women and 12 men (mean age, 57.4 years) received water with methylcellulose; and 35 women and 25 men (mean age, 64.6) received Readi-Cat 2%. There were no statistically significant differences between those who received Volumen and those who received either Readi-Cat 2% or water with methylcellulose with respect to the amount of distention that could be related to either patient age (*P* = .175) or sex (*P* = .445) (Table 2). There were no reported adverse effects. Volumen was successful in producing neutral contrast enhancement within the stomach, duodenum, and small bowel and facilitated the detection of disease (Fig 1). The uniformity and reproducibility of bowel distention and visualization could be appreciated in multiple patients (Fig 2).

Table 2

Classification of Patients according to Age and Sex

Parameter	Volumen	Water with Methylcellulose	Readi-Cat 2%	*P* Value*
Sex				.445
Male	15 (50.0)	18 (60.0)	35 (58.3)	
Female	15 (50.0)	12 (40.0)	25 (41.7)	
Age (y)†	58.1 ± 15.9	57.4 ± 17.1	63.6 ± 13.3	.175

Note.—Numbers in parentheses are percentages.

* *P* values represent two-sided significance levels from the Fisher exact and Kruskal-Wallis tests, which were used to assess the differences among contrast agents with respect to age and sex.

† Data are presented as the mean ± standard deviation.

Qualitative Analysis

For qualitative analysis (Table 3), the mean values for distention in the stomach (*P* = .013), duodenum (*P* = .006), jejunum (*P* = .029), and ileum (*P* = .140) were all significantly greater in group 1 than in group 2. The mean scores for visualization of anatomic detail in the duodenum (*P* = .003), jejunum (*P* = .024), and ileum (*P* = .010) were all significantly greater in group 1 than in group 2. There was a trend toward higher mean visualization scores in the stomach for patients in group 1, but this difference was not significant at the 5% level (*P* = .092). Of note is that, in each category, the scores for reader 1 were uniformly higher than those for reader 2. The scores for reader 2, however, were uniformly higher in group 1 than in group 2. We did not formally test the effect of glucagon administration between the two groups. The qualitative evaluations of the patients who did and those who did not receive glucagon did not appear to differ.

Quantitative Analysis

The results of the quantitative analysis are summarized in Table 4. For the quantitative assessment of distention in the duodenum, there was no significant relationship between the contrast agent used and the age (*P* = .667) or sex (*P* = .566) of the patient. There was a highly significant difference among the contrast agents (*P* = .001) in terms of maximal distention in the duodenum. The Tukey honestly significant difference showed that, after adjusting for age and sex, the maximal distention in the duodenum after administration of Volumen was significantly higher than that obtained after administration of either Readi-Cat 2% (adjusted honestly significant difference, *P* < .001) or water with methylcellulose (*P* = .014). The maximal distentions associated with Readi-Cat 2% and water with methylcellulose were not significantly different (*P* = .913).

Figure 1

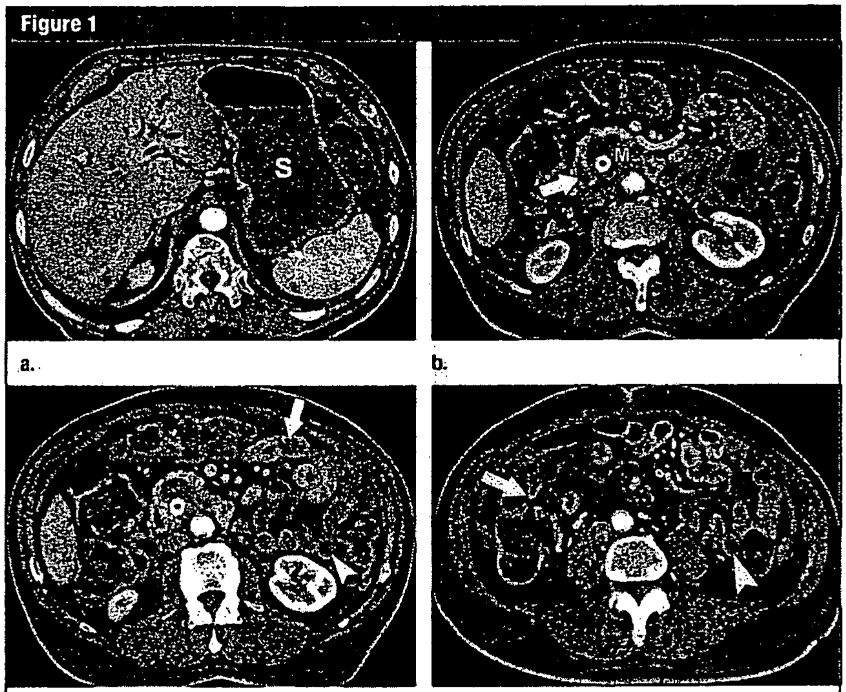

Figure 1: Transverse CT scans obtained in an 81-year-old man with known pancreatic adenocarcinoma after administration of Volumen. **(a)** Scan reveals well-distended stomach *(S)*. Mural features of gastric wall can be distinguished. No abnormality is seen in the uniformly thickened wall. **(b)** Scan reveals a mass *(M)* in the head of the pancreas. A metallic biliary stent is present within the common bile duct. Despite the mass, the duodenum is distended (arrow). Both walls can be visualized. In the left portion of the abdomen, neutral contrast enhancement is seen in the jejunal and proximal ileal loops. **(c)** Scan obtained at a slightly lower position than **b** demonstrates pancreatic mass. Jejunal wall and fold pattern can be easily distinguished (arrow). Note the visualized wall of the proximal ileal loops (arrowhead). **(d)** Scan obtained at level of the umbilicus reveals uniformly distended ileal loops (arrowhead). Terminal ileum is well distended as it enters the cecum (arrow).

There were highly significant differences between the sexes ($P = .003$) and among the contrast agents ($P < .001$) in terms of the maximal distention in the jejunum. Specifically, maximal distention in the jejunum was significantly higher for men (4.27 ± 1.10 [standard deviation]) than for women (3.70 ± 0.90). The Tukey honestly significant difference showed that, after adjusting for age and sex, the maximal distention in the jejunum after administration of Volumen was significantly higher than that obtained after administration of either Readi-Cat 2% (adjusted honestly significant difference, $P < .001$) or water with methylcellulose ($P < .001$). The maximal distentions associated with Readi-Cat 2% and water with methylcellulose were not significantly different ($P = .861$).

Figure 2

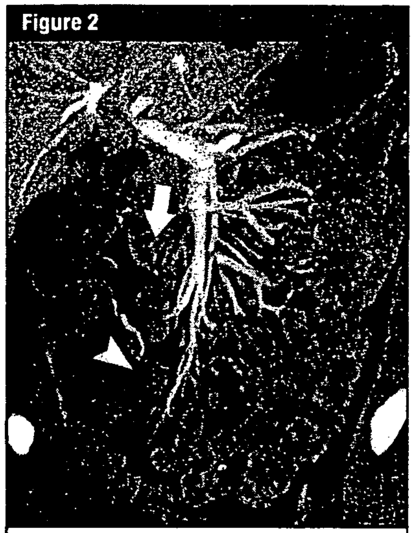

Figure 2: Coronal maximum intensity projection image obtained in 58-year-old woman displays both mesenteric arterial supply and venous drainage of small bowel. Note the uniform distention of the entire length of the small bowel. Folds in the duodenal sweep (arrow) can be seen. Terminal ileal region is displayed (arrowhead).

There were highly significant differences between the sexes ($P < .001$) and among the contrast agents ($P < .001$) in terms of maximal distention in the ileum. Specifically, the product of the bidimensional diameters in the ileum was significantly higher for men (mean, 3.17 ± 0.90) than for women (2.60 ± 0.60). The Tukey honestly significant difference showed that, after adjusting for age and sex, the maximal distention in the ileum after the administration of Volumen was significantly higher than that obtained after the administration of

Table 4

Results of Quantitative Analysis in Small Intestine for Each Contrast Agent

	Location		
Contrast Agent	Duodenum	Jejunum	Ileum
Volumen	4.97 ± 0.13	5.25 ± 0.13	3.84 ± 0.09
Readi-Cat 2%	4.37 ± 0.09	3.52 ± 0.09	2.49 ± 0.06
Water with methylcellulose	4.44 ± 0.13	3.61 ± 0.13	2.68 ± 0.09
P value			
Volumen vs Ready-Cat 2%	<.001	<.001	<.001
Volumen vs water with methylcellulose	.014	<.001	<.001
Readi-Cat 2% vs water with methylcellulose	.913	.861	.189

Note.—For quantitative analysis, a mixed-model least-squares regression that was adjusted for age and sex was used to calculate volume assessments (ie, the product of the cross-sectional diameters, as measured in square centimeters) that were associated with each of the three contrast agents in each of the three segments of the small intestine. Numbers are presented as the mean ± standard error of the mean.

Table 3

Results of Qualitative Analysis in Small Intestine for Each Group

	Distention				Visualization			
Group*	Stomach	Duodenum	Jejunum	Ileum	Stomach	Duodenum	Jejunum	Ileum
Group 1 ($n = 30$)								
Reader 1	3.7	3.4	3.5	3.5	3.9	3.5	3.5	3.5
Reader 2	3.2	2.7	2.7	2.8	3.3	2.7	2.6	2.8
Combined mean†	3.5	3.1	3.1	3.2	3.6	3.1	3.1	3.2
Group 2 ($n = 30$)								
Reader 1	3.1	2.6	3.0	2.9	3.2	2.6	2.9	2.9
Reader 2	2.7	2.2	2.0	2.1	2.9	2.2	1.9	2.0
Combined mean†	2.9	2.4	2.5	2.5	3.1	2.4	2.4	2.5
P value‡	.013	.006	.029	.140	.092	.003	.024	.010

Note.—For qualitative analysis, distention and visualization were scored by using a continuous five-point scale (0 = worst, 4 = best).

* For group 1, 1200 mL of Volumen was administered, and for group 2, 1200 mL of water with methylcellulose was administered.

† The combined mean was calculated as the arithmetic mean of both readers' responses.

‡ *P* values were calculated by using the Mann-Whitney test.

either Readi-Cat 2% (adjusted honestly significant difference, $P < .001$) or water with methylcellulose ($P < .001$). The maximal distentions associated with Readi-Cat 2% and water with methylcellulose were not significantly different ($P = .189$).

We did not formally test the effect of glucagon administration between the two groups. The quantitative evaluation of the patients who did and those who did not receive glucagon did not appear to differ.

Discussion

In the mid-1980s, negative oral contrast agents (12–14) (eg, air or carbon dioxide, which cause the contrast material–filled lumen to appear black and produce an attenuation measuring −200 HU or lower) and neutral oral contrast agents (eg, water or corn oil emulsions, which cause the contrast material–filled lumen to appear gray and produce an attenuation measuring either at or near that of water) began to be explored for use with abdominal CT (15). Although investigators noted a more precise visualization of the intestinal wall, the predominant use of these negative oral contrast agents was restricted to tumor staging (16–18) and did not approach replacing positive contrast agents.

An increased interest in the use neutral oral contrast agents has paralleled the widespread clinical use of multi–detector row CT scanners. The combination of rapid image acquisition and widespread use of eight to 16–detector row CT scanners, which provide high-quality multiplanar and three-dimensional volume-rendered images in any conceivable plane, produce remarkable images of a wide variety of intestinal abnormalities (3,19–21). The ability to visualize the bowel wall and to distend the lumen adds to the diagnostic capabilities of current abdominal CT examinations. The use of neutral luminal oral contrast agents combined with the volume capabilities of multi–detector CT scanners allow radiologists to routinely visualize the bowel and its vascular supply.

Patients referred for multi–detector row CT who consume 900–1000 mL of Volumen over a 20–30-minute period and who receive the final 200 mL (total volume of 1200 mL) immediately prior to the examination demonstrate significantly superior distention in all segments of the gastrointestinal tract and show significantly better depiction of anatomic detail in the duodenum, jejunum, and ileum, with slightly better anatomic visualization of gastric wall compared with that of patients who receive orally administered water with methylcellulose or standard barium suspension. Even though the volume of the oral contrast agent that was used in our study was less than the 1800 mL used by Wold and coworkers (5), we were still able to obtain excellent distention. Furthermore, our results show that we were able to achieve uniform and superior luminal distention compared with that achieved by administering positive contrast agents according to the established protocol. We did not modify our oral barium regimen to match the rapid drinking protocol used with neutral contrast agents; therefore, we cannot conclude that there would be a difference after similar modifications to the timing of oral administration of barium suspension at CT. It should be noted, however, that the rapid drinking of the neutral contrast agent achieved a major goal—that is, the reproducibly of uniform distention along the length of the gastrointestinal tract. Finally, we did not attempt to perform CT enterography by using Volumen nor did we have the ability to compare the performance of this contrast agent with that of water, as was used for this application.

The significantly improved performance of Volumen compared with that of water with methylcellulose in the duodenum, jejunum, and ileum may be related to the presence of stabilizing agents within Volumen that improve transit and diminish resorption across the intestinal wall. This effect is much less apparent when the stomach is maximally distended after administration of the immediate prescanning dose and by the fact that there is minimal water resorption from the stomach.

We did not formally test the potential benefits of glucagon between patients who did and those who did not receive this drug prior to examination. The numbers of patients in each group who did not receive glucagon or in whom administration was not documented (ie, seven patients in group 1 and seven patients in group 2) was small. The qualitative and quantitative results in these 14 patients were within the ranges of the entire patient cohort.

There are several collateral benefits available to clinical practice by using this contrast agent. First, in order for the contrast agent to perform optimally, at least two-thirds of the total volume (900–1000 mL) must be consumed over a 20–30-minute period, with the final third (200–300 mL) given when the patient enters the scanning suite. For the traditional oral contrast administration protocol, patients usually consumed the contrast agent over a 45–60-minute period. The more rapid cycle time could improve patient throughput without compromising diagnosis. A further potential benefit of using Volumen as a neutral contrast agent relates to the presence of the small quantity of barium in the suspension. This small amount of barium renders the overall attenuation of the lumen in the range of 20–40 HU. At this attenuation level, the luminal fluid is not so dense that it obscures the detail of the contrast-enhanced wall; however, because the contrast enhancement of the bowel wall appears slightly hyperdense compared with that of water, we expect that we can more easily distinguish adjacent cystic masses in the abdomen pelvis or retroperitoneum. We did not formally test this supposition.

At our institution, we currently use water with methylcellulose as the routine oral contrast agent for all patients who are suspected of having pancreatic or biliary disease. This is the reason why our study population was limited to patients with these clinical indications for CT. Therefore, we did not detect clinically important enteric disease in these individuals nor did we compare the findings of conventional barium examinations to those obtained with the reference standard in these patients.

Our sole purpose was to evaluate the degree of distention and the appearance of mucosal features along the bowel. Our ability to make diagnoses at CT in the 30 patients who received Volumen was not compromised. Currently at our institution, we have Volumen available as a contrast agent for all CT examinations. Although there are no specific contraindications for this contrast agent, it is generally recommended that water-soluble contrast agents should be used in patients suspected of having esophageal or intestinal perforation. The risk to patients who aspirate is equivalent to the risk associated with other barium suspensions.

Our quantitative analysis is limited by the fact that the widest wall-to-wall diameter is, at best, a surrogate measure of the overall distention within a segment of the gastrointestinal tract. We had no readily available method that would allow us to measure the volume of the entire segment of interest. Had we been able to render an entire segment of the alimentary canal in a cylindrical model for volume analysis, the differences may have become less apparent. The quantitative findings did, however, parallel those of the qualitative assessment, which evaluated the reader's impression of the entire segment.

We have found several drawbacks associated with this contrast agent. First, Volumen is optimally used in combination with an intravenous contrast agent because visualization of the contrast-enhanced bowel wall is necessary for recognition of a bowel loop. As one might imagine, this is especially important in thin patients. Therefore, we do not use this contrast agent for patients who are undergoing unenhanced CT examinations. Second, the absolute need for rapid drinking and ready access to the CT scanner once the contrast agent has been consumed requires that the radiology department carefully supervise the entire oral contrast agent dosing regimen. This may not be feasible in hospitals or emergency departments where oral contrast agent administration frequently is not directly controlled by the radiology department. Finally, it remains unclear if this contrast agent will provide sufficient endoluminal contrast enhancement to allow for the confident diagnosis of acute appendicitis. When coupled with intravenous contrast agents, positive oral contrast agents that distend the terminal ileum and cecum have been shown to be superior in facilitating the diagnosis of acute appendicitis (22). Should the appendix be surrounded by multiple distended loops that are filled with a neutral contrast agent and display a brightly enhanced wall, one can imagine this could confound rather than enhance diagnostic ability. We therefore still use our longstanding positive oral contrast material–based protocol when a patient is suspected of having acute appendicitis.

Despite the previously mentioned drawbacks, the results of our study provide a strong indication that excellent bowel distention and visualization can be obtained by using Volumen. The ability of this contrast agent to produce neutral contrast enhancement provides considerable advantages for emerging volume imaging with multi-detector row CT.

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